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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/004,808 | 12/07/2001 | H. William Bosch | 029318-0799 | 8203 |

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| EXAMINER | |
|---|---|
| TRAN, SUSAN T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | |

DATE MAILED: 11/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/004,808 | BOSCH ET AL. | |
| | Examiner | Art Unit | |
| | Susan T. Tran | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *14-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *39-50,105 and 106* is/are allowed.

6)☒ Claim(s) *14-38,51-104 and 107-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Receipt is acknowledged of applicant's Amendment filed 08/19/04.

### *Claim Rejections - 35 USC § 103*

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 14, 15, 1 7-21, 23, 24, 26, 27, 29-32, 34, 36, 37, 51, 52, 54-59, 61, 62, 64, 66-72, 74, 75, 93, 95, 101-104 and 107-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pace et al. (US 6177103 B1).

Pace teaches preparing a nanoparticulate composition of less than 2000 nm by adsorbing a cationic agent onto the surface of active agent particles (Col. 4, line 63 - Col. 5, line 21, Col. 5, line 60 -Col. 65, line 5., Col. 6 lines 34-67). Pace does not teach that the nanoparticles can be as large as 4000 nm but do teach anything below 2000 nm is acceptable.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to vary the particles size of active agents to be stabilize by cationic agents. One of ordinary skill in the art would have been motivated to do this to prepare stable particle of different drugs for different biological site delivery. The drug

and target sight will determine how small or large the particles should be for administration of the active with the same expected results. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the ad at the time the invention was made.

Claims 22, 28, 35, 47, 53, 60, 65, and 73 are rejected under 35 U.S.C. 1 O3(a) as being unpatentable over Pace et al. in combination with Liversidge et al. (US 5145684).

The teachings of Pace are discussed above. Pace does not expressly teach that the composition further comprises an excipient or that water is used as the dispersion medium. Liversidge teaches that such composition can further comprise a carrier (excipient) and that the dispersion medium can be water (Col. 16, Claims 12 and 14). At the time the invention was made, it would have been obvious to a person of ordinary skill in the ad to add an excipient such as a carrier to such a composition for administration of the composition.

One of ordinary skill in the art would have been motivated to do this to prepare various acceptable dosage forms for the active particles (i.e., injection carriers, oral carriers, or rectal carriers).

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 98-100 are rejected under 35 U.S.C. 1O3(a) as being unpatentable over

Pace et al. in combination with Cutie (US 5891420).

The teachings of Pace are discussed above. Pace does not expressly teach that the active agent is triamcinolone acetonide. Cutie teaches that triamcinolone acetonide is a known anti-inflammatory (Col. 2, lines 14-25).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the ad to use a known anti-inflammatory such as triamcinolone acetonide
in the composition of Pace. One of ordinary skill in the art would have been motivated to do this to prepare stable small particles (submicron) of anti-inflammatory for proper administration. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicant's arguments filed 08/19/04 have been fully considered but they are not persuasive.

Applicant argues that Pace does not teach compositions comprising crystalline particles. However, although Pace is silent as to the teaching of the crystalline particles, Pace teaches the compositions in particle having the claimed size ranges. Furthermore, applicant has not presented any unexpected result over the particles taught by Pace. Even furthermore, applicant's specification permits amorphous, semi-crystalline, or any combination of amorphous, and semi-crystalline (page 26, 3rd paragraph). Accordingly, there's no criticality in the crystalline particle being claimed.

Applicant's attention is called to column 3, lines 20-25, Pace teaches the particles are stable and do not appreciably flocculate or agglomerate, and can be formulated into pharmaceutical compositions exhibiting unexpectedly high bioavailability.

Applicant argues that Pace does not teach compositions comprising "poorly water-soluble active agent particles which are in a liquid state at or near room temperature". However, absent of evident on the contrary, the burden is shifted to applicant to provide support that the active agent particles taught by Pace is not in a liquid state at or near room temperature, since Pace teaches the claimed water-insoluble active agent (column 5, lines 23-67).

Applicant argues that Pace does not teach the active agent dissolved or dispersed in liquid droplets. Contrary to the applicant's argument, Pace teaches the surface modifier is dissolved in the liquefied gas along with the water-insoluble substance and expanded into a homogenized aqueous dispersion (column 5, lines 43-47, and example 1). Accordingly, Pace teaches the active agent dissolved or dispersed in liquid droplets.

In response to applicant's argument that Liversidge does not remedy the deficiencies of Pace, because the cited reference fails to teach every element of applicant's claimed invention, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d

413, 208 USPQ 871 (CCPA 1981). Liversidge is cited solely for the teaching of composition can further comprise a carrier (excipient) and that the dispersion medium can be water (Col. 16, Claims 12 and 14).

In response to applicant's argument that Cutie does not remedy the deficiencies of Pace, because the cited reference fails to teach every element of applicant's claimed invention, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Cutie is cited solely for the teaching of triamcinolone acetonide is a known anti-inflammatory (Col. 2, lines 14-25).

### *Claims Allowable*

Claims 39-50, 97, 105 and 106 are allowed.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-R from 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached at (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

THURMAN K. PAGE
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